distilled. The gummy residue was digested with *ca.* 5 *N* hydrochloric acid, and then treated with Norite and filtered. The red crystals which formed on chilling were filtered and recrystallized from ethanol, m.p. 226–228° (2.3 g.).

Anal. Calcd. for $C_{13}H_{13}ClN_2O$: Cl, 14.20; N, 11.22. Found: Cl, 13.98; N, 11.09.

BROOKLYN, N. Y.

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

The Preparation of Several Analogs of Amidone and Isoamidone[1]

BY F. F. BLICKE AND EU-PHANG TSAO[2,3]

RECEIVED NOVEMBER 10, 1953

One analog of Amidone and three analogs of isoamidone which contain hexa- or heptamethylenimino radicals as the basic substituents were synthesized. Reaction of diphenylacetonitrile and the necessary basic alkyl chlorides yielded the required nitriles which were converted into the final products by treatment with ethylmagnesium bromide. The structures of the nitriles were established by exhaustive methylation.

The object of this investigation was the preparation of several analogs of Amidone and isoamidone which contained hexamethylenimino and heptamethylenimino radicals as the basic portions of the molecule. The products obtained were 4,4-diphenyl-6-(1-hexamethylenimino)-3-heptanone (IV), 4,4-diphenyl-5-methyl-6-(1-hexamethylenimino)-3-hexanone (IX), 4,4-diphenyl-5-methyl-6-(1-heptamethylenimino)-3-hexanone (XVI) and a cyclic analog 1,1-hexamethylene-2,5-dimethyl-4,4-diphenyl-3-ketopiperidinium bromide (XI).

Compounds IV and IX were prepared in the following manner. Diphenylacetonitrile was condensed with β-(1-hexamethylenimino)-propyl chloride and sodamide to form a mixture of 2,2-diphenyl-4-(1-hexamethylenimino)-valeronitrile (I) and 2,2-diphenyl-3-methyl-4-(1-hexamethylenimino)-butyronitrile (VI). Advantage was taken of the greater solubility of the hydrochloride of I in isopropyl alcohol to separate the mixture into its components. Compounds I and VI reacted with ethylmagnesium bromide to form the desired ketones IV and IX.

In order to prove the structure of nitrile I, the nitrile was converted by methyl iodide into the quaternary iodide (II). The latter substance was heated with a mixture of silver oxide and water whereby 1,1-diphenyl-1-cyano-2-butene (III) and 1-methylhexamethylenimine were formed. Compound III was converted by lithium aluminum hydride into 1-amino-2,2-diphenyl-3-pentene and the latter substance was hydrogenated to 1-amino-2,2-diphenylpentane.

The structure of nitrile VI was established by conversion of the nitrile into the quaternary compound VII; when the latter substance was treated with silver oxide and water, 1,1-diphenyl-1-cyano-2-methyl-2-propene (VIII) and 1-methylhexamethylenimine were obtained. Reduction of VIII with lithium aluminum hydride yielded 1-amino-2,2-diphenyl-3-methyl-3-butene which was hydrogenated to form 1-amino-2,2-diphenyl-3-methylbutane.

Compound IX was converted into the hydrobromide (IX·HBr) which after bromination yielded X. After treatment of X with ammonia water, a product was obtained which we believe is 1,1-hexamethylene-2,5-dimethyl-4,4-diphenyl-3-ketopiperidinium bromide (XI). Compound IV was submitted to the same series of reactions. In this instance interaction of V with ammonia water yielded a crystalline substance but the analytical data did not correspond to that calculated for a piperidone analogous to XI.

When diphenylacetonitrile was condensed with β-(1-heptamethylenimino)-propyl chloride and sodamide, a mixture of the basic nitriles, XII and XIII, was obtained. The mixture was treated with hydrochloric acid, and the two hydrochlorides were then separated by the use of isopropyl alcohol.

The structures of nitriles XII and XIII were also established by exhaustive methylation. Compound XII yielded butene III and 1-methylheptamethylenimine, while compound XIII was decomposed to propene VIII and 1-methylheptamethylenimine.

The ketone XVI, as well as the cleavage product XVII, was obtained in the usual manner from nitrile XIII.

Tested in the Parke, Davis and Company laboratories, it was found that compounds IX and XVI were less active than Amidone; in the case of XVII, there was uncertainty regarding the analgesic quality of action; analgesic activity, if present, in IV and XI was confounded with side effects.

Experimental Part

2,2-Diphenyl-3-methyl-4-(1-hexamethylenimino)-butyronitrile (VI) and 2,2-Diphenyl-4-(1-hexamethylenimino)-valeronitrile (I).—Diphenylacetonitrile (58 g., 0.3 mole), dissolved in 230 cc. of benzene, was added dropwise to a stirred suspension of 15 g. of pulverized sodamide in 150 cc. of benzene. The mixture was stirred at 40° for 1 hour, 53 g. (0.3 mole) of β-(1-hexamethylenimino)-propyl chloride[4] added dropwise and the mixture was stirred and heated at 50° for 10 hours. Water was added, the organic layer was separated and the aqueous layer was extracted with benzene. The solvent was removed from the combined extract and the organic layer and the residue distilled; b.p. 168–170° (0.01 mm.), yield 92.6 g. (93%).

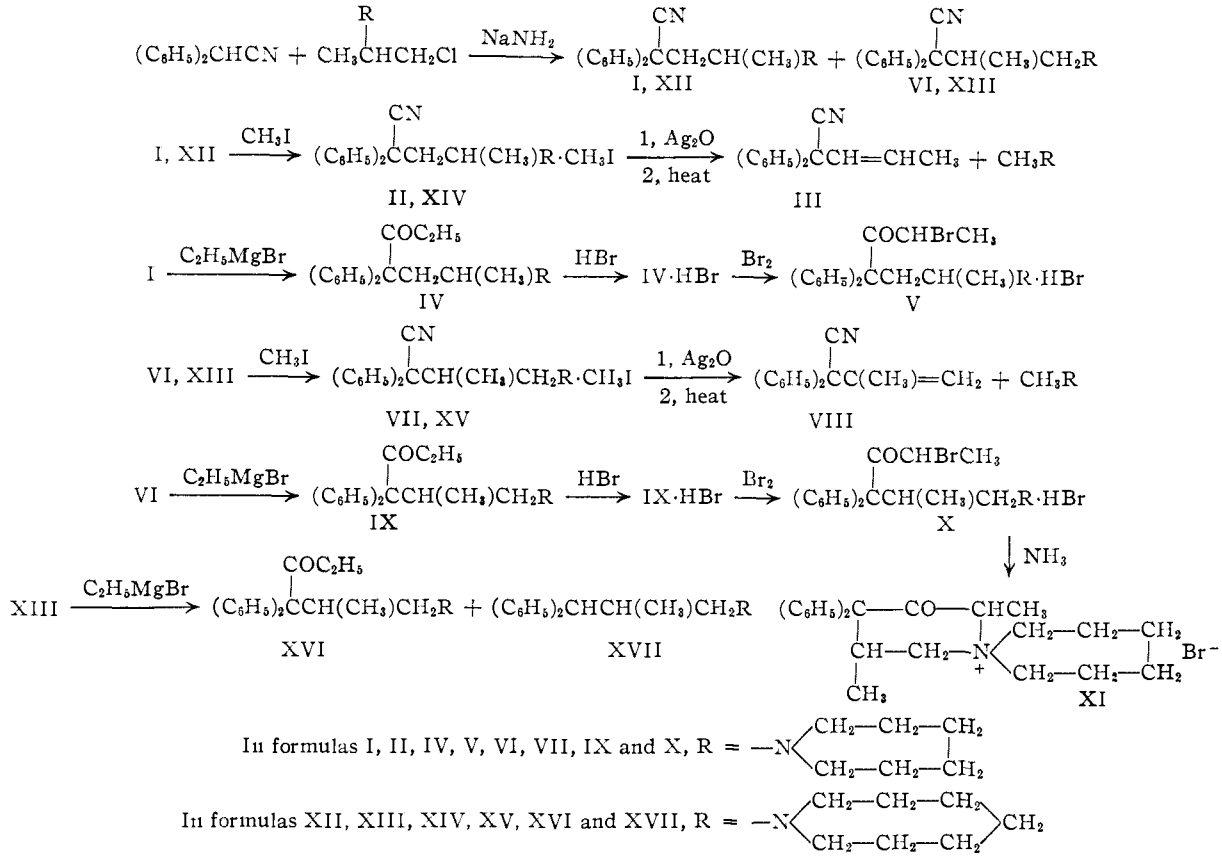
A mixture of the hydrochlorides of VI and I precipitated when an ethereal solution of the base was treated with hydrogen chloride. The mixture was dissolved in the smallest possible amount of hot isopropyl alcohol. The hydrochloride of VI, which precipitated from the cold solution (A), melted at 234–235° after recrystallization from isopropyl alcohol. Analytical data indicated that the hydro-

(1) Abstracts of Papers, 123rd Meeting of the American Chemical Society, Los Angeles, Calif., March 15–19, p. 14L.

(2) This paper represents part of a dissertation submitted by Eu-Phang Tsao in partial fulfillment of the requirements for the Ph.D. degree in the University of Michigan, 1952.

(3) Parke, Davis and Company Fellow.

(4) N. J. Doorenbos, Dissertation, University of Michigan, 1953.



chloride crystallizes from isopropyl alcohol or from acetone with solvent of crystallization which can be removed at 110°. The solvent-free salt was analyzed.

Anal. Calcd. for $C_{23}H_{29}N_2Cl$: C, 74.87; H, 7.92; N, 7.60; Cl, 9.61. Found: C, 74.87; H, 7.88; N, 7.39; Cl, 9.67.

In order to liberate the base, the hydrochloride was dissolved in methanol and the solution made alkaline with aqueous sodium hydroxide. The base was extracted with benzene and the solvent removed; m.p. 77–78° after recrystallization from petroleum ether.

The solution (A) from which the hydrochloride of VI had been removed was concentrated to a small volume. Ether was added to the hot solution until it became turbid. The hydrochloride of I precipitated from the cold mixture; m.p. 194–195.5° after recrystallization from ether–isopropyl alcohol.

Anal. Calcd. for $C_{23}H_{29}N_2Cl$: C, 74.87; H, 7.92; N, 7.60; Cl, 9.61. Found: C, 74.97; H, 7.78; N, 7 80; Cl, 9.61.

The base, liberated from the hydrochloride, is a viscous liquid; b.p. 169–172° (0.05 mm.).

From 141.5 g. of a mixture of the two isomers (VI and I), 67 g. of VI and 62 g. of I were obtained.

Structure Determination of VI.—A mixture of 15 g. of VI, 40 cc. of isopropyl alcohol and 40 cc. of methyl iodide was refluxed for 16 hours. The precipitated methiodide VII was recrystallized from aqueous methanol; m.p. 217–218.5°, yield 20.5 g.

Anal. Calcd. for $C_{24}H_{31}N_2I$: I, 26.74. Found: I, 26.89.

The methiodide (20 g.), 500 cc. of water and 200 cc. of methanol were heated on a steam-bath, stirred vigorously and 15 g. of silver oxide was added in small portions. The mixture was heated for 30 minutes, cooled, filtered and the filtrate evaporated to dryness *in vacuo*. The residue was heated with 2 g. of solid potassium hydroxide in a distillation flask for 25 minutes at 145° (bath temperature). The oily distillate was dissolved in ether, the solution dried with sodium sulfate and then treated with hydrogen chloride. The precipitated 1-methylhexamethylenimine hydrochloride melted at 180.5–182.5°[5] after recrystallization from acetone.

Anal. Calcd. for $C_7H_{16}NCl$: Cl, 23.74. Found: Cl, 23.92.

Water was added to the residue in the distillation flask and the mixture was extracted with ether. The extract was washed with dilute hydrochloric acid to remove any basic material, then washed with water, dried over sodium sulfate and the solvent removed. The crystalline residue, 1,1-diphenyl-1-cyano-2-methyl-2-propene (VIII), melted at 65–66°[6]; yield 9.4 g.

Compound VIII (9.4 g.) was treated with 2 g. of lithium aluminum hydride in ether and the mixture was refluxed for 5 hours and then treated with 4 cc. of water. The 1-amino-2,2-diphenyl-3-methyl-3-butene obtained (8.0 g.) boiled at 140–145° (1.5 mm.).

The butene (8.0 g.) was dissolved in 30 cc. of methanol and hydrogenated in the presence of 0.1 g. of platinum oxide catalyst, under an initial pressure of 45 pounds for 9 hours. 1-Amino-2,2-diphenyl-3-methylbutane (6.2 g.), which boiled at 143–146° (2 mm.), was obtained. 1-[(2,2-Diphenyl-3-methyl)-butyl]-3-phenylthiourea precipitated when 1 g. of the butane, dissolved in 15 cc. of petroleum ether (30–40°), was treated with 1 g. of phenyl isothiocyanate; m.p. 157–158°.[7]

Structure Determination of I.—The methiodide (II) was prepared from 15 g. of I, 40 cc. of isopropyl alcohol and 40 cc. of methyl iodide; m.p. 181–182.5° after recrystallization from methanol, yield 17 g.

Anal. Calcd. for $C_{24}H_{31}N_2I$: I, 26.74. Found: I, 26.92.

The methiodide (16 g.), dissolved in a mixture of 120 cc. of methanol and 400 cc. of water, was heated with 12 g. of silver oxide. The quaternary hydroxide was degraded in the described manner. The reaction products were 1-methylhexamethylenimine (hydrochloride, m.p. 181–

(5) G. R. Toy (Dissertation, University of Michigan, 1951) found 181.5–183.5°.

(6) E. M. Schultz, C. M. Robb and J. M. Sprague, THIS JOURNAL, **69**, 2454 (1947), found 63–64°.

(7) Reference 6, m.p. 157–158°.

182.5°) and 1,1-diphenyl-1-cyano-2-butene (III); b.p. 146–150° (1.5 mm.), yield 5.5 g.

Compound III (5.5 g.) was reduced with lithium aluminum hydride to 1-amino-2,2-diphenyl-3-pentene; b.p. 137–141° (1 mm.), yield 5.2 g.

The pentene (5.2 g.) was reduced catalytically, with the aid of platinum oxide, to 1-amino-2,2-diphenylpentane; b.p. 108–109.5° (0.2 mm.), yield 4.7 g. The benzoyl derivative melted at 146–147°[8] and the thiourea at 182–183°.[9]

4,4-Diphenyl-5-methyl-6-(1-hexamethylenimino)-3-hexanone (IX).—2,2-Diphenyl-3-methyl-4-(1-hexamethylenimino)-butyronitrile (VI, 33.2 g., 0.1 mole), dissolved in 60 cc. of toluene, was added to a stirred solution of ethylmagnesium bromide prepared from 18 g. of ethyl bromide, 4 g. of magnesium and 80 cc. of ether. After distillation of the ether, the mixture was stirred and refluxed for 20 hours. The mixture was treated with ammonium chloride solution, the organic layer separated and the aqueous layer extracted with benzene. The solvents were removed from the combined organic solutions and the residue was refluxed with a mixture of 80 cc. of 48% hydrobromic acid and 30 cc. of methanol for 46 hours. The hydrobromic acid was removed by distillation, the residue neutralized with sodium hydroxide solution and then extracted with benzene. The solvent was removed from the solution and the residue was distilled; b.p. 169–174° (0.05 mm.), yield 32.1 g. (88.3%).

The hydrochloride was recrystallized from isopropyl alcohol; m.p. 203–204°.

Anal. Calcd. for $C_{25}H_{34}ONCl$: C, 75.06; H, 8.57; N, 3.50; Cl. 8.86. Found: C, 75.12; H, 8.77; N, 3.51; Cl, 8.93.

The hydrobromide precipitated when hydrogen bromide was passed into an ethereal solution of the base; m.p. 219–220.5°.

Anal. Calcd. for $C_{25}H_{34}ONBr$: N, 3.15; Br, 17.98. Found: N, 3.23; Br, 17.95.

2-Bromo-4,4-diphenyl-5-methyl-6-(1-hexamethylenimino)-3-hexanone Hydrobromide (X).—A solution of 4.0 g. (0.025 mole) of bromine in 10 cc. of acetic acid was added, dropwise, to a stirred boiling solution of 11.1 g. (0.025 mole) of the hydrobromide of IX. The mixture was refluxed for 30 minutes, the solvent was removed under reduced pressure and the residue was recrystallized from isopropyl alcohol–ether; yield 11.0 g. (84%), m.p. 180–181° dec. after recrystallization from ethanol.

Anal. Calcd. for $C_{25}H_{33}ONBr_2$: N, 2.68; Br, 30.55. Found: N, 2.67; Br, 30.26.

1,1-Hexamethylene-2,5-dimethyl-4,4-diphenyl-3-ketopiperidinium Bromide (XI).—Ammonia water (1.5 cc.) was added to a suspension of 5.2 g. of X in 25 cc. of water and the mixture was stirred for 20 hours. The product was filtered, washed with water and recrystallized from ethanol; m.p. 229–230° dec., yield 2.5 g. (80%).

Anal. Calcd. for $C_{25}H_{32}ONBr$: C, 67.86; H, 7.29; N, 3.17; Br, 18.06. Found: C, 67.52; H, 7.36; N, 3.36; Br, 18.09.

4,4-Diphenyl-6-(1-hexamethylenimino)-3-heptanone (IV).—2,2-Diphenyl-4-(1-hexamethylenimino)-valeronitrile (I, 29.5 g., 0.089 mole), dissolved in 60 cc. of toluene, was added to ethylmagnesium bromide prepared from 18 g. of ethyl bromide, 4 g. of magnesium and 80 cc. of ether. Subsequent operations were the same as those described above. The product boiled at 166–170° (0.05 mm.); yield 27.5 g. (85.4%).

The hydrochloride was recrystallized from ethyl acetate; m.p. 157–158.5°.

Anal. Calcd. for $C_{25}H_{34}ONCl$: C, 75.06; H, 8.57; N, 3.50; Cl, 8.86. Found: C, 74.67; H, 8.58; N, 3.50; Cl, 8.96.

The hydrobromide was recrystallized from ethyl acetate; m.p. 144–145.5°.

Anal. Calcd. for $C_{25}H_{34}ONBr$: Br, 17.98. Found: Br, 17.85.

2-Bromo-4,4-diphenyl-6-(1-hexamethylenimino)-3-heptanone (V).—A solution of 2.2 g. of bromine in 5 cc. of acetic acid was added to a boiling solution of 6.2 g. (0.014 mole) of the hydrobromide of IV in 20 cc. of acetic acid. The mixture was refluxed for 25 minutes. After removal of the solvent the residue was recrystallized from ethyl acetate; m.p. 169–171° dec., yield 5.9 g. (80%).

Anal. Calcd. for $C_{25}H_{33}ONBr_2$: N, 2.68; Br, 30.55. Found: N, 2.70; Br, 30.62.

2,2-Diphenyl-3-methyl-4-(1-heptamethylenimino)-butyronitrile (XIII) and 2,2-Diphenyl-4-(1-heptamethylenimino)-valeronitrile (XII).—A solution of diphenylacetonitrile (78 g., 0.4 mole) in 300 cc. of benzene was added, dropwise, to a stirred suspension of 18 g. (0.47 mole) of pulverized sodamide in 150 cc. of benzene. The mixture was stirred for 2 hours at room temperature, then 76 g. (0.4 mole) of β-(1-heptamethylenimino)-propyl chloride[4] was added and the mixture was heated at 50° for 6 hours. Water was added, the organic layer separated and the aqueous layer extracted with benzene. The combined organic solutions were shaken with 60 cc. of concd. hydrochloric acid. The precipitate was dissolved in the smallest possible amount of hot isopropyl alcohol. The hydrochloride of XIII separated from the cold solution (B) with solvent of crystallization; yield 84.3 g. (45%). After recrystallization from isopropyl alcohol, the product melted at 218.5–220°. After removal of the solvent of crystallization at 110°, the product was analyzed.

Anal. Calcd. for $C_{24}H_{31}N_2Cl$: C, 75.26; H, 8.16; N, 7.32; Cl, 9.26. Found: C, 75.17; H, 8.09; N, 7.51; Cl, 9.26.

The base was liberated from the hydrochloride; m.p. 101.5–102.5° after recrystallization from methanol.

The hydrobromide melted at 230–231.5° after recrystallization from methanol–ethyl acetate.

Anal. Calcd. for $C_{24}H_{31}N_2Br$: Br, 18.69. Found: Br, 18.70.

The hydriodide melted at 228–229° after recrystallization from methanol.

Anal. Calcd. for $C_{24}H_{31}N_2I$: I, 26.74. Found: I, 26.95.

The methiodide (XV, 21 g.) was obtained when the base (15 g.) was heated with methyl iodide in methanol for 12 hours; m.p. 221–222° dec. after recrystallization from methanol.

Anal. Calcd. for $C_{25}H_{33}N_2I$: I, 25.97. Found: I, 26.02.

The alcoholic solution (B), from which the hydrochloride of XIII had been removed, was treated with ether whereupon the hydrochloride of XII precipitated; yield 41 g., m.p. 188–189.5° after recrystallization from isopropyl alcohol–ether.

Anal. Calcd. for $C_{24}H_{31}N_2Cl$: C, 75.26; H, 8.16; N, 7.32; Cl, 9.26. Found: C, 74.76; H, 8.12; N, 7.18; Cl, 9.23.

The mother liquor was made alkaline, extracted with ether and the extract dried over sodium sulfate. Upon distillation, 14 g. of product was obtained; b.p. 168–172° (0.04 mm.). The product was then converted into the hydrochloride. Since the latter melted at 188–189.5°, the distillate must have been XII.

The methiodide XIV melted at 183–184° after recrystallization from methanol–ethyl acetate.

Anal. Calcd. for $C_{25}H_{33}N_2I$: I, 25.97. Found: I, 26.12.

Structure Determination of XII.—The methiodide (XIV, 13 g.), dissolved in a mixture of 100 cc. of methanol and 200 cc. of water, was heated with 9 g. of silver oxide and the quaternary hydroxide was degraded. The 1-methylheptamethylenimine obtained was converted into the hydrochloride; m.p. 162–163.5°[10] after recrystallization from methanol–ethyl acetate.

Anal. Calcd. for $C_8H_{18}NCl$: Cl, 21.66. Found: Cl, 21.66.

The 1,1-diphenyl-1-cyano-2-butene (III, 4.5 g.) produced boiled at 138–140° (1 mm.); and when reduced with lithium aluminum hydride yielded 4.1 g. of 1-amino-2,2-diphenyl-3-pentene; b.p. 137–139° (1 mm.). Hydrogenation of the latter compound produced 1-amino-2,2-diphenylpentane; b.p. 138–139° (1 mm.); yield 3.8 g. The thiourea derivative melted at 182–183°.

Structure Determination of XIII.—The methiodide XV (18.5 g.) was converted in the manner which has been de-

(8) Reference 6, m.p. 146–147°.

(9) Reference 6, m.p. 179–180°.

(10) Reference 4, m.p. 163–164°.

scribed, into 1-methylheptamethylenimine (hydrochloride, m.p. 162–164°) and 1,1-diphenyl-1-cyano-2-methyl-2-propene (m.p. 65–66°). The latter substance was reduced to 1-amino-2,2-diphenyl-3-methyl-3-butene and this product was hydrogenated to 1-amino-2,2-diphenyl-3-methylbutane (4.8 g.). The thiourea derivative melted at 157–158°.

4,4-Diphenyl-5-methyl-6-(1-heptamethylenimino)-3-hexanone (XVI).—The nitrile XIII (17.3 g.), dissolved in 40 cc. of toluene, was added to ethylmagnesium bromide which had been prepared from 9.0 g. of ethyl bromide, 2.0 g. of magnesium and 50 cc. of ether. After the ether had been removed, the mixture was refluxed for 6 hours, treated with ammonium chloride solution, the organic layer was separated and the aqueous portion extracted with benzene. The solvents were removed from the combined organic layer and extract and the residue distilled; b.p. 158–163° (0.05 mm.), yield 13.0 g. An ethereal solution of the distillate was treated with hydrogen chloride. The precipitated mixture of hydrochlorides was dissolved in hot isopropyl alcohol. 1,1-Diphenyl-2-methyl-3-(1-heptamethylenimino)-propane (XVII) hydrochloride precipitated from the cold solution; yield 3.0 g., m.p. 195.5–196.5° after recrystallization from methanol–ethyl acetate. This compound was also synthesized in a separate experiment which is described below.

Anal. Calcd. for $C_{23}H_{32}NCl$: C, 77.14; H, 9.01; N, 3.92; Cl, 9.93. Found: C, 77.13; H, 9.05; N, 3.96; Cl, 9.99.

Upon the addition of ether to the mother liquor, the dihydrochloride of 3-imino-4,4-diphenyl-5-methyl-6-(1-heptamethylenimino)-hexane precipitated in an impure form; m.p. 146–148° dec.

Anal. Calcd. for $C_{25}H_{38}N_2Cl_2$: Cl, 15.80. Found: Cl, 14.84.

When this product was refluxed with 30 cc. of constant boiling hydrochloric acid for 40 hours, 4,4-diphenyl-5-methyl-6-(1-heptamethylenimino)-3-hexanone hydrochloride (9.5 g., 46%) was obtained; m.p. 199–200° after recrystallization from methanol–ethyl acetate.

Anal. Calcd. for $C_{26}H_{36}ONCl$: C, 75.44; H, 8.77; N, 3.38; Cl, 8.57. Found: C, 75.54; H, 8.74; N, 3.28; Cl, 8.52.

1,1-Diphenyl-2-methyl-3-(1-heptamethylenimino)-propane (XVII).—A mixture of 4.2 g. of 2,2-diphenyl-3-methyl-4-(1-heptamethylenimino)-butyronitrile, 1.9 g. of sodamide and 40 cc. of xylene was refluxed for 12 hours. After the addition of water the organic layer was separated, the solvent removed and the residue distilled; b.p. 158–161° (1 mm.), yield 3.8 g. (98%). The hydrochloride melted at 195–196°; mixed m.p. 195–196°.

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ALABAMA POLYTECHNIC INSTITUTE]

Preparation of Some Substituted 2-Methyl-3-indoleacetic Acids[1,2]

BY FRANK J. STEVENS AND DON H. HIGGINBOTHAM

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2-Methyl-5-bromo-, 2-methyl-7-bromo-, 2-methyl-5,7-dibromo-, 2,7-dimethyl-5-bromo-, 2-methyl-4-chloro-7-methoxy- and 2-methyl- (4 or 6)-chloro-3-indoleacetic acids have been prepared from the properly substituted phenylhydrazones of ethyl levulinate by the Fischer indole synthesis. 2-Methoxy-5-chlorophenylhydrazine, the hydrochloride and acetyl derivatives have been prepared.

The preparation of some substituted 2-methyl-3-indoleacetic acids has been reported.[3] The activity of these compounds as plant growth regulators varies with the nature of the substituting groups and their positions in the indole nucleus.[3,4] The work presented here is part of a general program to increase the number of such derivatives available for phytological investigations correlating structure with activity. The new acids were prepared from the appropriately substituted ethyl levulinate phenylhydrazones using a modified Fischer synthesis.[5] The phenylhydrazones were prepared from ethyl levulinate and the substituted phenylhydrazine which was liberated from its hydrochloride in aqueous solution by sodium acetate. In the preparation of the substituted phenylhydrazine hydrochlorides it was found that an excellent method of purification consisted of liberating the free base from the crude phenylhydrazine hydrochlorides, extracting with ether and reprecipitating the hydrochloride from the dried ether solution with hydrogen chloride. The free substituted phenylhydrazines are not very stable in air, while the hydrochlorides can be stored for long periods without decomposition. All of the phenylhydrazines with the exception of 2-methoxy-5-chlorophenylhydrazine have been characterized previously as free bases but not in all cases as hydrochlorides. The melting point of 2-methyl-4-bromophenylhydrazine hydrochloride was found to be considerably higher than that reported in the literature.[6] Anhydrous zinc chloride was used as catalyst in the ring closure and an atmosphere of carbon dioxide was maintained, since the phenylhydrazones decompose in air. Only one product was isolated from the cyclization of ethyl levulinate, *m*-chlorophenylhydrazone, although both 2-methyl-4-chloro- and 2-methyl-6-chloro-3-indoleacetic acids are possible. Fox and Bullock obtained two products from the cyclization of the *m*-chlorophenylhydrazone of β-formylpropionic acid with ethanolic sulfuric acid.[7] The position of the halogen in the single compound obtained is under investigation.

Experimental

All m.p.'s (capillary) are uncorrected.

Substituted Phenylhydrazine Hydrochlorides.—All of the phenylhydrazine hydrochlorides were prepared by Hewitt's procedure,[8] except the product was allowed to precipitate overnight. The precipitate was filtered, and washed once with concd. hydrochloric acid. The product was purified

(1) From the thesis by Don H. Higginbotham presented to the Graduate School in partial fulfillment of the requirements for the M.S. Degree.

(2) This research was supported in part by the Grant-in-Aid Program of the Alabama Polytechnic Institute.

(3) F. J. Stevens and S. W. Fox, THIS JOURNAL, **70**, 2263 (1948).

(4) F. J. Stevens, Ph.D. thesis, Iowa State College, 1947.

(5) E. Fischer, *Ber.*, **19**, 1563 (1886).

(6) L. Michaelis, *ibid.*, **26**, 2190 (1893).

(7) S. W. Fox and M. W. Bullock, THIS JOURNAL, **73**, 2756 (1951).

(8) J. T. Hewitt, *J. Chem. Soc.*, **59**, 209 (1891).